

stably incorporated into the genome, wherein the construct comprises a promoter for expression of the construct in a mammalian cell and a region encoding an A $\beta$ -containing protein, wherein the promoter is operatively linked to the region,

wherein the region comprises DNA encoding the A $\beta$ -containing protein, wherein the A $\beta$ -containing protein consists of all or a contiguous portion of a protein selected from the group consisting of

APP770 bearing a mutation in one or more of the amino acids selected from the group consisting of amino acid 669, 670, 671, 690, 692, and 717, APP751 bearing a mutation in one or more of the amino acids selected from the group consisting of amino acid 669, 670, 671, 690, 692, and 717, and APP695 bearing a mutation in one or more of the amino acids selected from the group consisting of amino acid 669, 670, 671, 690, 692, and 717,

wherein the A $\beta$ -containing protein includes amino acids 672 to 714 of human APP,

wherein the region encoding an A $\beta$ -containing protein does not consist of a combination of APP cDNA encoding exons 1-6 and 9-18 and genomic APP sequences encoding introns 6, 7 and 8, and exons 7 and 8,

wherein the promoter mediates expression of the construct such that A $\beta$ tot is expressed at a level of at least 30 nanograms per gram of brain tissue of the mouse when it is two to four months old, A $\beta$ 1-42 is expressed at a level of at least 8.5 nanograms per gram of brain tissue of the mouse when it is two to four months old, APP and APP combined are expressed at a level of at least 150 picomoles per gram of brain tissue of the mouse when it is two to four months old, APP $\beta$  is expressed at a level of at least 40 picomoles per gram of brain tissue of the mouse when it is two to four months old, and mRNA encoding the A $\beta$ -containing protein is expressed to a level at least twice that of mRNA encoding the endogenous APP of the transgenic mouse in brain tissue of the mouse when it is two to four months old;

wherein the transgenic mouse develops plaques that stain with Congo red; and detecting or measuring the Alzheimer's disease marker such that any difference between the marker in the transgenic mouse, or by cells derived from the transgenic mouse, and the marker in a transgenic mouse to which the compound has not been administered, or by cells derived from the transgenic mouse to which the compound has not been administered, is observed,

wherein an observed difference in the marker indicates that the compound has an effect on the marker.

33. A method for screening compounds for an effect on an Alzheimer's disease marker comprising

a) administering the compound to be tested to a transgenic mouse, or cells derived from the transgenic mouse, wherein the transgenic mouse has a nucleic acid construct stably incorporated into the genome, wherein the construct comprises a promoter for expression of the construct in a mammalian cell operatively linked to a region of the construct encoding a human amyloid precursor protein,

wherein the region of the construct encoding a human amyloid precursor protein is selected from the group consisting of APP770 cDNA bearing a mutation in the codon encoding amino acid 669, 670, 671, 690, 692, 717, or a combination of these mutations; APP751 cDNA bearing a mutation in the codon encoding amino acid 669, 670, 671, 690, 692, 717, or a combination of these mutations; APP695 cDNA bearing a mutation in the codon encoding amino acid 669, 670, 671, 690, 692, 717, or a combination of these mutations; APP695, APP751, or APP770 cDNA truncated at amino acid 671 or 685; APP cDNA truncated to encode amino acids 646 to 770 of APP; a combination cDNA/genomic APP gene construct; a combination cDNA/genomic APP gene construct bearing a mutation in the codon encoding amino acid 669, 670, 671, 690, 692, 717, or a combination of these mutations; and a combination cDNA/genomic APP gene construct truncated at amino acid 671 or 685;

wherein A $\beta$  is expressed at a level of at least 50 ng/g brain tissue in the transgenic mouse when the transgenic mouse is three months of age;

wherein the transgenic mouse develops plaques that stain with Congo red; and detecting or measuring the Alzheimer's disease marker such that any difference between the marker in the transgenic mouse, or by cells derived from the transgenic mouse, and the marker in a transgenic mouse to which the compound has not been administered, or by cells derived from the transgenic mouse to which the compound has not been administered, is observed,

wherein an observed difference in the marker indicates that the compound has an effect on the marker.

Please cancel claims 28 and 56 without prejudice.